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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/556,910	06/20/2007	**Dennis Rylatt**	063373-5053-US	1610

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EXAMINER	
KASTEN, ROBERT J	

ART UNIT	PAPER NUMBER
1795	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/556,910	RYLATT ET AL.	
	Examiner	Art Unit	
	ROBERT KASTEN	1795	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 November 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This is the first non final action on the merits.

Claims 1-30 are pending. Claims 4-16 and 18-30 have been amended. No new matter has been added.

Drawings

1. New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because both drawings are not of sufficient quality. The grainy quality of Figure 1 makes it difficult to discern any actual structure. The grainy quality of the graph in Figure 2 makes it very difficult to determine which bar corresponds to RBC and WBC, even with the legend as part of the graph. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 29-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the present case, there is

insufficient antecedent basis for the limitation of "the cell concentration" in claim 29. Addition of a step to claim 1 requiring administration of a cell sample at a certain concentration could correct the 112, 2nd paragraph issue here.

Further, claims 29-30 fail to provide units for the cell concentration ranges (10^5, 10^{10}, 10^6, 10^8). Examiner has construed these concentrations to be in terms of cells/mL, in other words that a cell sample would have a concentration of 10^5 cells/mL.

Finally, regarding claims 29-30, it is unclear in what part of the system that the cells have the claimed concentration. In other words, are the cells of this concentration in the first sample chamber or second sample chamber, and are they there at the concentration before separation, after separation or both?

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1-2, 4-7, 9-12, 16-25 are rejected under 35 U.S.C. 102(e) as being anticipated by CONLAN et al. (US 2003/0029725), from here on referred to as CONLAN.

Concerning Claim 1, CONLAN teaches a method for the separation of molecules (abstract) comprising the following steps:

- Providing an electrophoresis apparatus of claim 4 (Claim 25, (a)).
- Providing a sample to the apparatus (Claim 25, (b)), wherein the sample can be a mixture [0057] of different molecules of interest [0090], and the samples may comprise various cell types (microbial cultures, cell culture media, plant products, etc) [0090]
- Applying an electric potential between the electrodes [0053] causing movement of one micromolecule from one sample to another sample chamber across the membrane [0073]

The apparatus of claim 4 comprises the following structural features from Figure 11:

- a first electrolyte chamber 11 (anode buffer compartment) [0053]
- a second electrolyte chamber 12 (cathode buffer compartment) [0053]
- a first sample chamber 16 between the electrolyte chambers [0054]
- a second sample chamber 17 between the electrolyte chambers [0055]
- the second sample chamber 17 disposed adjacent the first sample chamber 16 [0020], though they are separated by an ion-permeable separation membrane 13 [0054]
- a second ion-permeable membrane 18 disposed between the first electrolyte chamber 11 and first sample chamber 16 [0054]

- A third ion-permeable membrane 19 disposed between the second electrolyte chamber 12 and second sample chamber 17 [0055]
- Electrodes 14 and 15 provided in the buffer compartments [0053].

Concerning Claim 2, CONLAN teaches that the sample may be a microbial culture [0090], which inherently contains viable cells.

Concerning Claim 4, CONLAN teaches that at least two cell populations (microbial culture and plant products (which can inherently contain plant cells)) can be contained in the sample [0090].

Concerning Claim 5, CONLAN teaches that in use, an applied electric potential across the membrane allows migration of at least one of the micromolecules in a sample from a first chamber across the separation membrane to a second chamber [0073]. Further, CONLAN teaches a method in which removal of contaminants is achieved while retention of target product is maintained in the device [0072].

Concerning Claim 6, CONLAN teaches that movement of the micromolecules across the membrane occurs upon application of the electric potential [0073].

Concerning Claim 7, convective mixing is inherently prevented by the membranes of CONLAN.

Concerning Claim 9, CONLAN teaches that the first barrier (separation barrier) membrane have a molecular weight cut-off (analogous to pore size) of 5 to 1000 kDa [0079].

Concerning Claim 10, CONLAN teaches that the other barrier membranes have a molecular weight cut-off (analogous to pore size) of less than 5000 Da [0081].

Concerning Claims 11-12, CONLAN teaches that the separation membrane can be composed of polyacrylamide [0064] and have a pore size of 10 kDa [0113].

Concerning Claims 16, CONLAN teaches that the separation membrane (first barrier membrane) has a molecular weight cut-off of 1000 kDa [0079] and the restriction membranes (second and third membranes) have a cut-off of 5000 Da (5 kDa) [0081].

Concerning Claim 17, CONLAN teaches that the restriction membranes are formed from polyacrylamide [0061-0062].

Concerning Claim 18-19, CONLAN teaches that 83% of a sample (Azorubine) is recovered after using the prior art device [0119]. This percentage is inherently "substantially unchanged" as required by the claim, since the presence of 83% of the sample was determined by absorbance at a specific wavelength characteristic to that sample. This absorbance measuring process is used for gaining meaningful insight into the presence and/or concentration of a sample would necessitate functional, unaltered versions of the sample.

Concerning Claim 20, CONLAN teaches a sample being added to the device, separated, and then removed [0073]. This reads on a batch process.

Concerning Claim 21-22, CONLAN teaches that the voltage can be anywhere from 0 to 5000 V [0070].

Concerning Claim 23-24, CONLAN teaches that the field strength (for the preferred 6 cm long apparatus [0066]) may be anywhere from 0 - ~833 V/cm:

$$E = V/d \text{ [0066]}$$

$$E = (0\text{-}5000 \text{ V}) / 6 \text{ cm [0070]}$$

$$E = 0 - \sim 833 \text{ V/cm}$$

Concerning Claim 25, CONLAN teaches that the sample may be separated for 45 minutes [0119].

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 3, 8 and 26-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over CONLAN.

Concerning Claim 3, CONLAN teaches that cells can be separated by the method of claim 2 [0090].

CONLAN does not expressly teach that cells like erythrocytes, leukocytes, bone marrow, etc. may be separated by the prior art process.

The specific cells the device is used to separate are a matter of intended use and the claim of one cell over another is a matter of engineering design choice. CONLAN essentially teaches this point in [0064], specifically that the actual size of the cut-off (in other words the pore size) is dependent on the molecules in the sample mixture. In other words, the device and method can be tailored to work with whatever sized molecule the user wished to separate. Absent evidence to the contrary, the method of CONLAN is capable of performing the claimed separation and it would have been obvious to one of

ordinary skill in the art to perform the method on the claimed cell types as a matter of experimental design.

Concerning Claim 8, CONLAN teaches method with all the steps of claim 1.

CONLAN does not expressly teach that the electric potential is maintained until a molecule reaches the user's desired purity.

The purity of the sample is a matter of obvious experimental design choice. The claim of a "desired purity" necessarily means that this is a claim to optimization, as what is desired must necessarily differ from user to user and depend on the characteristics of the sample, such as availability, intended use, etc. One of ordinary skill in the art would have known that to achieve the desired separation of sample, the separation force (electric potential) must be applied until the separation is achieved. Therefore, at the time of the invention, it would have been obvious to one of ordinary skill in the art to apply electric potential as long as was necessary to achieve the desired separation.

Concerning Claim 26, CONLAN teaches that the sample may be separated for 45 minutes [0119].

CONLAN does not expressly teach that the separation run for about 10 minutes.

The selection of a specific time duration is obvious because the time of separation is a result effective variable with easily quantifiable results. One of ordinary skill in the art would know that longer separations would lead to more sample migrating across the membrane. However, one of ordinary skill in the art

would have also known that there is a diminishing return as the sample is separated, meaning that while, hypothetically, the first 5 minutes of separation might yield 70% separation, an additional 5 minutes might only yield an additional 5%, and yet another 5 minutes only an additional 2%. Therefore, the choice of one separation duration over another is an optimization process in which the user must determine at what point "enough" sample has been separated that additional separation is unnecessary/inefficient.

Concerning Claim 27, CONLAN teaches that the concentration of the selected buffers can be about 10 mM to about 400 mM [0091]. CONLAN also teaches that the choice of the buffer and the buffer concentration depend on the intended use of method, since both of these parameters affect the movement of molecules across the membrane [0091]. "In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists." *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976)" (2144.05, (I)).

Concerning Claim 28, CONLAN teaches that the buffer used in the separation method is Tris Borate [0091]. Further, CONLAN teaches that the composition of the buffer used may be changed depending on the specific separation to be performed [0091].

CONLAN does not expressly teach that the buffer be any of the claimed buffers.

However, the teaching of CONLAN that the buffer can be altered to whatever buffer is suitable for the process [0091] would lead one of ordinary skill

in the art to know that the use of any of the claimed buffers over Tris Borate is a matter of design choice. Since CONLAN uses Tris Borate in microbial cultures [0090], this buffer is known to be cell-compatible, as is required by the claim. Therefore, one of ordinary skill in the art would have known that from the device of CONLAN, a cell-compatible buffer should be used, and further that a specific cell-compatible buffer different from Tris Borate could be used if said other buffer exhibited advantages in specific separation conditions. Such a buffer substitution would be a matter of engineering design choice.

Concerning Claims 29-30, CONLAN does not expressly teach the concentrations of the samples. However, because CONLAN anticipates the method in claim 1 and therefore performs the method on the same material as required by claim 1, one of ordinary skill in the art would be able to logically discern that the concentration of the sample could be within the claimed range. Further, the optimization of the sample concentration is well within the skill of one of ordinary skill in the art since the behavior of a membrane in response to sample concentration is well within the skills of one of ordinary skill in the art. A sample concentration that is too high for the membrane will lead to fouling of the membrane, leading to an unnecessary amount of membrane maintenance, replacement, and possible loss of sample. However, a concentration that is too low could lead to unnecessarily long experimental duration, it which the separating the sample could take many times longer than necessary without achieving higher separation. Therefore, at the time of the invention, it would

have been *prima facie* obvious to one of ordinary skill in the art to operate in the method of CONLAN with a cell concentration in the claimed ranges.

9. Claims 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over CONLAN in view of WU (US 6,824,995), from here on referred to as WU.

Concerning Claim 13, CONLAN teaches a method with all the steps of claim 12.

CONLAN does not expressly teach that the separation barrier be provided and made of polycarbonate.

However, WU teaches a polycarbonate membrane as part of an apparatus for determining the mobility of cancer cells (col. 17, lines 44-46).

The motivation for using a polycarbonate membrane like that of WU in the device of CONLAN is the reasonable expectation of success and the behavior of the membrane. One of ordinary skill in the art would have expected success because the WU teaches that the cells are still able to pass through the membrane (col. 17, lines 47-50), making the membrane at least useful in processes in which smaller target molecules were to be separated from larger molecules unable to migrate through the membrane. Further, WU teaches that the cells that did migrate across were still viable (able to establish growth below the membrane, col. 17, lines 50-51), meaning that the polycarbonate would be unlikely to destroy the samples in the device of CONLAN. Finally, the teaching that smaller pore sizes in the membrane slow the progress of cells across the

membrane (col. 17, lines 51-53) implies that the membrane is capable of being a functionally similar barrier to the polyacrylamide one of CONLAN, one that substantially prevents the sample from migrating across until an electric potential is applied. Therefore, at the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to use a polycarbonate membrane like in WU as the membrane in CONLAN because of this reasonable expectation of success and non-detrimental interaction with the sample.

Concerning Claims 14-15, CONLAN does not expressly teach the claimed pore sizes.

However, the choice of one pore size over another is a matter of obvious engineering design choice. CONLAN essentially teaches this point in [0064], specifically that the actual size of the cut-off (in other words the pore size) is dependent on the molecules in the sample mixture. In other words, depending on the intended use of the method and attached apparatus, the pore size would have been chosen so that the desired separation of molecules was performed. Separation of smaller molecules would necessitate smaller pore sizes, larger molecules would necessitate larger pore sizes, etc. Therefore, at the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to fabricate the membrane of CONLAN with any pore size claimed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT KASTEN whose telephone number

is (571)270-7598. The examiner can normally be reached on Mon-Thurs, 8am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Sines can be reached on 571-272-1263. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/R. K./
Examiner, Art Unit 1795

/Brian J. Sines/

Supervisory Patent Examiner, Art Unit 1795